

**ABSTRACT**

The present invention provides novel methods of preventing, diagnosing, and treating Critical Limb Ischemia (CLI), using eNOS polypeptides and polynucleotides to modulate eNOS activity in cells.

Wild-type and mutant eNOS polypeptides, and polynucleotides encoding such polypeptides, are  
5 provided for use in the methods of the present invention. The eNOS mutant polypeptides of the present invention have at least one mutation corresponding to a site in a functional domain of a mammalian eNOS that is phosphorylated in cells.